REMARKS

The Office Action mailed January 30, 2001, has been received and reviewed. Claims 1-17, 23-32, 53 and 59-78 are currently pending in the application. Claims 23-32, 53 and 74-78 were withdrawn from consideration. Claims 1-17 and 59-73 stand rejected. Applicants have canceled claims 1, 2, 4, 5, 7, 9, 11, 12, 15, 59, 61, 63, 64, 65, 67, 68, and 71 and amended claims 3, 6, 10, 13, 14, 16, 17, 62, 66, 69, 70, 72, and 73, and respectfully request reconsideration.

A Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequences And/or Amino Acid Sequence Disclosures was attached to, and referenced in, the Office Action. Applicants have complied with the notice to comply by furnishing a computer readable format version of the Sequence Listing and the required statement along with this Office Action.

35 U.S.C. § 102 Rejections

In the Office action, claims 1, 2, 4, 5, 7, 9, 11, 12, 15, 59-61, 63-65, 67, 68, and 71 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,518,913 to Massie et al. While Applicants respectfully disagree with the rejection, these claims have all been cancelled without prejudice, or disclaimer, in order to expedite the process, rendering these rejections moot.

35 U.S.C. § 112 Rejections

Claims 13 and 69 were rejected in the Office Action as assertedly lacking enablement under 35 U.S.C. § 112, first paragraph. The Office Action directed applicants to comply with the deposit rules with respect to the PER.C6 cells deposited at the ECACC and to provide a statement that all

restrictions on the availability to the public of the deposited material will be irrevocably removed upon granting of a patent on the instant application. Applicants have amended the specification to comply with the deposit rules, by this amendment, and have provided the required statement, which accompanies this amendment. Applicants respectfully submit this rejection is thus fully resolved and should be withdrawn.

Claims 1 to 17 and 59 to 73 were rejected in the Office Action as indefinite under 35 U.S.C. § 112, second paragraph. Applicants have cancelled some of these claims, rendering this rejection moot as to them. Applicants have further amended some of these claims and respectfully submits that the remaining claims, as amended are definite and that the rejection should be accordingly withdrawn.

In the Office Action, claims 1, 2, 6, 17, 62 and claims dependent therefrom were rejected as indefinite for vagueness with respect to use of the phrase "welding together" two nucleic acid molecules, based upon the terminology not being art recognized. Claims 1 and 2 have been cancelled, rendering the rejection moot as to those claims. Claims 6, 10, 13, 14, 17, 62, 66, 69, 70, 72 and 73 are rewritten in independent form and contain this terminology.

As stated in the MPEP at § 2173.01:

> A fundamental principle contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art. Applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the Court in *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought.

The phrase "welding together" is explained in the specification. One example is found at page 52, lines 1 to 5 of the application. Here it is explained that welding together means faithfully joining two strands of nucleic acid, and may be accomplished by any means capable of such a joining. Preferably, the welding together consists of one homologous recombination. Applicants have thus defined this phrase in accordance with 35 U.S.C. § 112, second paragraph.

The term welding is defined as "the action or process of making or joining with a weld" (Merriam-Webster, Inc., Webster's Third New International Dictionary of the English Language, 1986, Page 2594). One definition of the term weld is "2: to unite closely or intimately: join closely or inseparably: form into or as if into a single unit"(Ibid). The plain meaning of the phrase "welding together" as applied to two nucleic acids is thus the joining of two separate nucleic acids into one single nucleic acid. This meaning is the consistent with that used by applicants. Applicants use of this phrase therefore is obviously not contrary to the accepted usage. Applicants respectfully submit that the phrase is not vague, but is instead fully explained and supported in the specification, and consistent with the common meaning and usage of the phrase. Applicants respectfully requeststhis rejection be withdrawn and that amended claims 6, 10, 13, 14, 17, 62, 66, 69, 70, 72 and 73 be allowed.

Claims 3, 6, 10, 12-14, 17, 59, 62, 66, 68- 70, 72 and 73 and dependent claims were rejected under 35 U.S.C. 112, second paragraph in the Office Action. Claims 12, 59, and 68 have been cancelled, rendering this rejection moot as to those claims. The Office Action states the recitation of nucleic acid sequences from adenoviruses or nucleic acids of interest or "derivatives and/or analogues thereof" is vague. The Office Action inquires if these terms include non-adenoviral

sequences, if any, which could perform the same functions as an adenoviral packaging signal or adenoviral ITRs.

Explanations of functional fragments and derivatives or analogues with respect to some embodiments of the present invention are found throughout the specification. One example is located at page 43, line 31 to page 44, line 2. There, it is explained that while certain embodiments of vectors created by the claimed methods may preferably include the adenoviral E3 region, it is not necessary that such embodiments retain the entire region, so long as the function of reducing host immune response against infected cells is retained. From this example, it can be seen that the derivatives and/or analogues thereof encompass such fragments, derivatives and analogues that retain the function of the pertinent nucleic acid sequences. In fact, the rejected terminology is merely redundant, as such fragments derivatives and analogues are already encompassed by the term "nucleic acid sequence of interest" that is already found in these claims. Applicants have thus amended these claims to remove the redundancy, and respectfully submit that amended claims 3, 6, 10, 13, 14, 17, 62, 66, 69, 70, 72 and 73 are definite and supported in the specification. Applicants respectfully request these claims be allowed.

Claim 2 was rejected in the Office Action as indefinite for vagueness with respect to the term "essentially only one" homologous recombination event. The Office Action states that it "is unclear what 'essentially only one' homologous recombination event encompasses...." Claim 2 has been cancelled rendering this rejection moot as to that claim. Amended claims 62, 66, 69, 70, 72 and 73 are now rewritten in independent form and contain the elements of canceled claim 2, including the element of "essentially only one" homologous recombination event.

At page 45, line 28 through page 46 line 2 of the application, the meaning of the term "essentially only one" is defined in specification, with respect to homologous recombination events. The specification states:

> "With 'essentially only one' is meant that the overlapping sequences in each nucleic acid include essentially only one continuous sequence whereby homologous recombination leading to the generation of a functional adenovirus may occur. Within the continuous sequence, the actual number of homologous recombination events may be greater than one."

Applicants thus respectfully submit this term is clear and unambiguous as it is fully explained by, and supported in, the specification. Applicant respectfully submits this rejection should be withdrawn and amended claims 62, 66, 69, 70, 72 and 73 be allowed.

Claims 4,13, 60, 69 and the claims dependent therefrom were rejected in the Office Action as vague for reciting the claimed methods performed in a "functional part, derivative or analogue" of a cell. Claims 4 and 60 have been canceled rendering this rejection moot as to them. Claims 13, 14 and 69 have been amended to remove any vagueness. Applicants respectfully submit that as amended claims 13, 14 and 69 are definite and supported by the specification. Applicants respectfully request this rejection be withdrawn and the claims allowed.

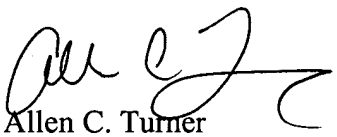
A rejection of claim 59 for vagueness was contained in the Office Action. Applicant has canceled claim 59, rendering this rejection moot.

Claims 7 and 63 were rejected for indefiniteness in the Office Action. These claims have been cancelled by this amendment, rendering these rejections moot.

Conclusion

Claims 3, 6, 10, 13, 14, 17, 62, 66, 69, 70, 72, and 73 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, he is respectfully invited to contact Applicant's undersigned attorney.

Respectfully Submitted,



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Enclosures: Version of Amendments with Markings to Show Changes Made

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please amend Page 27, line 23 so the paragraph identified as 5) appears as follows:

5) After transfection of HER cells with construct pIG.E1A.E1B (FIG. 4), seven independent cell lines were established. These cell lines were designated PER.C1, PER.C3, PER.C4, PER.C5, PER.C6, PER.C8 and PER.C9. PER denotes PGK-E1-Retinoblasts. These cell lines express E1A and E1B proteins, are stable (*e.g.*, PER.C6 for more than 57 passages), and complement E1-defective adenoviral vectors. Yields of recombinant adenovirus obtained on PER cells are a little higher than obtained on 293 cells. One of these cell lines (PER.C6) [has been] was deposited at the ECACC under number 96022940 on July 2, 2001.

IN THE CLAIMS:

Please cancel claims 1, 2, 4, 5, 7, 9, 11, 12, 15, 59, 61, 63, 64, 65, 67, 68, and 71, without prejudice.

Please amend the claims to appear as follows:

3. (Two times amended) [A method according to claim 1] A method for generating an adenoviral vector comprising welding together two nucleic acid molecules wherein both of said nucleic acid molecules comprise only one adenovirus inverted terminal repeat or a [functional] part, derivative, and/or analogue thereofhaving the function of an inverted terminal repeat, said two nucleic acid molecules further comprising partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof.

6. (Two times amended) A method [according to claim 5,] for generating an adenoviral vector comprising welding together in a mammalian cell two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; wherein said nucleic acid molecules are not capable of replicating in said mammalian cell prior to said welding together.

10. (Amended) A method [according to claim 9, wherein said] for generating an adenoviral vector comprising welding together two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; wherein at least one of said nucleic acid molecules comprises an adenovirus inverted terminal repeat made essentially free of other

nucleic acid on one side using a restriction enzyme that acts on a site which is not present in adenoviral vector nucleic acid in said nucleic acid molecule.

13. (Two times amended) A method [according to claim 4, wherein said cell is] for generating an adenoviral vector comprising welding together; in a PER.C6 cell (ECACC 96022940) [or a functional derivative, and/or analogue thereof] , two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof.

14. (Two times amended) A method [according to claim 4, wherein] for generating an adenoviral vector comprising welding together, in a cell, two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and nucleic acid sequence of interest or functional parts thereof; said nucleic acid in said cell further [comprises] comprising a nucleic acid sequence encoding an adenoviral E2-region and/or an adenoviral E4-region protein.

16. (Two times amended) A method [according to claim 1, wherein] for generating an adenoviral vector comprising welding together two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; at least one of said molecules [comprises] comprising an adenoviral capsid protein encoding nucleic acid derived from two different adenovirus serotypes.

17. (Two times amended) A method [according to claim 1, wherein said] for generating an adenoviral vector comprising welding together [of said] two nucleic acid molecules [leads to the] wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal [,] and a nucleic acid encoding at least one adenoviral E1-region protein, at least one adenoviral E2-region encoded protein and/or at least one adenoviral E4-region encoded protein and a nucleic acid sequence of interest or functional parts [, derivatives and/or analogues] thereof and wherein at least one of said E1-region encoded proteins is under transcriptional control of a conditionally active promoter.

62. (Amended) A method [according to claim 61,wherein said] for generating an adenoviral vector comprising welding together, through homologous recombination in a mammalian cell, two nucleic acid molecules [are] incapable of replicating in said mammalian cell prior to said welding together; said two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences allow essentially only one homologous recombination which leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof.

66. (Amended) A method [according to claim 65, wherein] for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences allow essentially only one homologous recombination which leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; at least one of said nucleic acid molecules provided to said cell comprises an adenovirus inverted terminal repeat which, on one side, is made essentially free of other nucleic acid on one

side using a [said] restriction enzyme that acts on a site which is not present in adenoviral vector nucleic acid in said nucleic acid molecule.

69. (Amended) A method [according to claim 2 , wherein said cell is] for generating an adenoviral vector comprising welding together, through homologous recombination in a PER.C6 cell (ECACC 96022940) [or a functional derivative, and/or analogue thereof] , two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences allow essentially only one homologous recombination which leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof.

70. (Amended) A method [according to claim 2, wherein] for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences allow essentially only one homologous recombination which leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; said nucleic acid [in said cell] further [comprises] comprising a nucleic acid sequence encoding an adenoviral E2-region and/or an adenoviral E4-region protein.

72. (Amended) A method [according to claim 2, wherein] for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences allow essentially only one homologous recombination which leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; at least one of said molecules [comprises] comprising an adenoviral capsid protein encoding nucleic acid derived from two different adenovirus serotypes.

73. (Amended) A method [according to claim 2, wherein said] for generating an adenoviral vector comprising welding together [of said] through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences allow essentially only one homologous recombination which leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal, a nucleic acid encoding at least one adenoviral E1-region protein, at least one adenoviral E2-region encoded protein and/or at least one adenoviral E4-region encoded protein and a nucleic acid sequence of interest or functional parts [, derivatives and/or analogues] thereof and wherein at least one of said E1-region encoded proteins is under transcriptional control of a conditionally active promoter.